A Phase 3, Randomized, Parallel-Group, Multi-Center, Multi-National Study for the Evaluation of Efficacy and Safety of (LMW) Heparin/Edoxaban Versus (LMW) Heparin/Warfarin in Subjects With Symptomatic Deep-Vein Thrombosis (DVT) and or Pulmonary Embolism (PE).

Treatment of venous thromboembolism, the Hokusai VTE Study

Background: Edoxaban is an oral direct factor Xa inhibitor. It is currently being studied for prevention of stroke in atrial fibrillation and for prevention/treatment of venous thromboembolism (VTE - DVT/PE). Edoxaban has a 10 000 fold increased selectivity for factor Xa in relation to thrombin. Edoxaban has been associated with statistically significant dose-dependent reductions in VTE in several studies.

Question to answer: Will edoxaban be more efficacious than LMWH/heparin/warfarin in prevention and treatment or recurrent VTE?

Trial Design	Prospective, double-blind, modified intention to treat. n=8292. Time on Treatment = 3 to12 months; follow-up for 12 months. (All patients: initial therapy with enoxaparin or UF heparin for up to 5 days) Edoxaban and warfarin was then administered in randomized, double blind fashion. (n=4143 heparin/edoxaban and n = 4149 heparin/warfarin (INR 2.0-3.0)		
Primary Endpoint	Symptomatic recurrent venous thromboembolism (composite of DVT, non-fatal PE, and fatal PE).		
Trial Results (Primary Efficacy)	Edoxaban (n=130 patients with recurrent VTE, 3.2%)	Warfarin (n=146 patients with recurrent VTE, 3.5%)	HR = 0.89; 95% CI (0.70-1.13) P=0.001 for non-inferiority.
Take Away: Edoxaban, given one time daily (post initial treatment with LMWH/heparin) was non-inferior compared to quality standard treatment and was associated with much less bleeding within a large group of patients with VTE (including patients with severe pulmonary embolism.			

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